The Veterinary Record

FOUNDED BY WILLIAM HUNTING, F.R.C.V.S., 1888.

No. 3. JANUARY 18, 1941. VOL. 53.

THE OCCURRENCE OF JAAGZIEKTE IN ENGLAND

F. BLAKEMORE and T. J. BOSWORTH

FROM THE INSTITUTE OF ANIMAL PATHOLOGY, CAMBRIDGE

Robertson (1904) described a disease of sheep in South Africa which was characterised by coughing and accelerated respiration. In fatal cases these symptoms increased in severity until the least movement caused the animals to pant and lie down completely exhausted. At this stage the sheep looked as though they had been over-driven and it was this appearance that gave rise to the name jaagziekte, from the Dutch " jaagen," to drive, and " ziekte," a disease. The lesions were characteristic and consisted of greyish nodules in the lung tissue which, in many respects, resembled soft cancerous growths.

Cowdry (1925) studied the pathology of the disease and formed the opinion that the first change was a local congestion of the alveolar capillaries. Later, macrophages and lymphocytes accumulated in the interalveolar tissue and the former penetrated in large numbers into the alveolar lumina. There was also extensive proliferation of the alveolar linings and the newly formed cells either assumed a papillomatous arrangement or remained attached to the alveolar walls. At a certain stage the proliferations were said to resemble closely those described by M'Fadyean (1920) in verminous pneumonia in sheep. Cowdry and Marsh (1926) also reported a striking similarity between the lesions of jaagziekte and those of progressive pneumonia described as affecting sheep in Montana.

Further interest was stimulated in the subject when Dungal *et al.* (1938) reported the occurrence in Iceland of a disease described as epizootic adenomatosis which they considered to be the same as jaagziekte. The disease has evidently been spreading increasingly throughout the country during recent years, resulting in the death of 50 to 80 per cent. of the sheep in some flocks. This mortality is much higher than the death rate of 1·5 per cent. reported in South Africa by Mitchell (1915) and the greater incidence amongst Icelandic sheep is attributed to the conditions existing on the island which necessitate the folding together of large numbers in the autumn and close housing during the winter.

The Icelandic disease runs a chronic course and in its early stages may be overlooked. In advanced cases the symptoms are striking since, in addition to respiratory distress, there is increased bronchial secretion and fluid pours out of the nostrils in quantities up to 50 c.c. when the head is inclined. Moist rales can also be detected by auscultation and in severe cases they may be audible when standing near the sheep.

The position regarding the occurrence of jaagziekte in Britain is somewhat obscure, but M'Fadyean (1937) has produced evidence to show that it has existed here. In articles published in 1894 and 1920 this author drew attention to a peculiar condition of the lungs of sheep characterised by great thickening of the alveolar walls and a remarkable transformation of the alveolar epithelium in what were then regarded as cases of verminous pneumonia. Later, when comparing his sections with those from cases of jaagziekte, he found that the changes described by him were identical with those produced in that disease and concluded that it must have been in existence in this country for some considerable time. Its presence here seems to be by no means generally recognised, however, and no clinical description of it has yet been published. In view of this, it was decided to record the following account of an outbreak which was brought to our notice.

DESCRIPTION OF THE OUTBREAK

In July, 1938, our attention was drawn to an obscure pneumonic condition affecting sheep in a Norfolk flock. Several deaths had occurred and although the sheep had been obtained from a number of sources the losses were limited to a batch of 100 cross-bred ewes purchased in Scotland, as shearlings the previous summer. During July six sheep died from the condition. Since then there have been occasional cases of the disease in the flock but it has shown no tendency to spread to the same extent as it does in Iceland.

Two of the affected sheep were examined during life. They were emaciated, were breathing rapidly and appeared to be in great distress, especially when exercised. Rales were pronounced and audible without auscultating the lungs. The most characteristic sign was the tendency for fluid to run from the nostrils when the head was inclined. This fluid, which was of a clear, serous character, could be collected repeatedly at short intervals in amounts varying from 40 to 80 c.c. and the total quantity excreted daily must have been very great. There was no elevation of temperature and the animals fed, although the appetite was indifferent. They were both killed after being kept under observation for a few days.

MORBID ANATOMY

On autopsy the changes were essentially the same in each case. The characteristic lesions were found

to be confined to the lungs and smaller bronchi. The lungs were increased in size and in one animal weighed 10 lb. Extensive areas of consolidation, somewhat spherical in shape and measuring up to 3 in. across, were found in the tissue. A striking feature of these lesions was that they were water-logged, and when squeezed much fluid exuded. They were greyish in colour and merged gradually into the surrounding normal lung (Fig. 1). In both cases the lower portions of the lungs were principally involved, but the cut surface of the lung revealed smaller foci of a similar nature scattered throughout the apparently normal tissue. While the general appearance resembled a neoplastic condition no metastases were found in the thoracic lymphatic glands, which were only slightly enlarged and oedematous. In one animal there was an adhesive pleurisy but the changes were not marked and the pleura was not greatly thickened.

Histologically the changes were identical with those described by Cowdry (1925) in the South African disease and by Dungal *et al.* (1938) in Icelandic pneumonia.

In the more lightly affected parts the lesions were seen as scattered foci (Fig. 2) lying in lung tissue of normal appearance except that the inter-alveolar tissue was thickened in places by the presence of macrophages and lymphocytes. Typical foci were composed of groups of alveoli in which the epithelium showed changes which have been described as characteristic of jaagziekte. The cells were cubical or columnar in shape and appeared to have arisen as the result of transformation of the normal flat lining epithelial cells. In some instances they remained attached to the alveolar walls giving a definite adenomatous appearance but more often showed a tendency to proliferate as a single layer supported by delicate connective tissue, thus assuming a papillomatous arrangement. Around some of these foci were seen alveoli packed with macrophages, some of which contained two nuclei, while many showed clear vacuoles in their cytoplasm and others the remains of ingested neutrophils or occasionally of red blood corpuscles. In the grossly affected parts, which had presumably been formed by the fusion of a number of originally discrete foci, the areas of epithelial proliferation (Fig. 3) were very extensive and were interspersed with other areas in which the reaction took the form of infiltration with either macrophages or neutrophils or a mixture of both (Fig. 4). There was also evidence here of developing fibrosis. The majority of the bronchioles failed to show any marked change, apart from the presence of some desquamated cells and neutrophils in the lumen but in some of them the lining cells had proliferated giving rise to papilla-like outgrowths attached to the inner wall. Extensive peri-bronchiolar infiltration with cells, mainly lymphocytes, was apparent in some of the sections.

The Aetiology of Jaagzjekte

Very little is known regarding the aetiology of jaagziekte and all attempts to transmit it experimentally in South Africa have failed. In Iceland the disease is believed to be contagious and Dungal and his co-workers were able to transmit it by housing infected sheep with healthy stock. They failed, however, to demonstrate an infective micro-organism or transmit it by the inoculation of bacteria-free filtrates.

Cowdry (1925) considered it possible that the disease may be due to a single and specific virus and suggested that a variety of predisposing and exciting factors operating over a considerable period of time may assist its development. He also pointed out that in early cases the epithelial proliferation into the alveoli resembled the changes which sometimes follow influenzal pneumonia. De Kock (1929) was unable to transmit jaagziekte by close contact to sheep whose resistance had been lowered by lung-worm infection, bleeding, *Strongyloides papillosus* infection, splenectomy, and the application of tar on the skin. He considered the condition to be of a neoplastic nature and classified it as multiple papilliform cystadenoma.

In his early reports, before the disease he was interested in had been compared with jaagziekte, M'Fadyean considered that the epithelial proliferation may have been due to stimulation by lungworms. The Icelandic disease is also usually complicated by a heavy infestation with *Muellerius capillaris* but Dungal *et al.* (1938) considered that the parasites were not primarily concerned with the causation of the lesions. Our own findings support the view that typical proliferative changes in the epithelium can occur in the absence of parasites for we failed to find any macroscopical or microscopical evidence of the presence of lungworms in either of our cases. Moreover, Dr. Lapage, who kindly examined the lungs for larvae by mincing and screening the material, reported a negative result. As bacteriological examination failed to reveal any bacteria of pathological significance, a small scale experiment was undertaken to ascertain whether the disease could be transmitted. Four sheep were inoculated intratracheally with a suspension of affected lung tissue. They were kept under observation for six months and remained normal throughout the experiment.

Four other sheep which were treated in exactly the same manner with material from a case in Iceland, kindly sent to us in the frozen state by Professor Dungal, were kept under observation for periods ranging from 8 to 14 months, during which they remained healthy and in prime condition. On *post-mortem* examination, the lungs of both batches of animals appeared to be normal and showed no histological changes suggestive of jaagziekte in the form of epithelial proliferation or even of cellular infiltration of the inter-aveolar tissue which was described by Cowdry (1925) as an early stage in the development of the lesions. It would seem, therefore, that sheep cannot readily be infected by the injection of such material.

Discussion

In view of the occurrence of this sporadic outbreak of jaagziekte it becomes important to consider the general position regarding the disease in this country. The evidence brought forward by M'Fadyean would indicate that the disease has existed here for many years but the symptoms and lesions are so striking that it is difficult to explain the absence of clinical reports relating to its occurrence. On the other hand, it may be that the sheep in this country are relatively resistant and that the disease is usually characterised by the presence of small areas of epithelial proliferation which do not result in the development of the clinical condition. Further evidence on this point is clearly needed for it is interesting to note that De Kock (1929) found small lesions in a considerable

FIG. 1.
Cut surface of affected lung with advanced lesions in upper half and less extensive infiltration below.

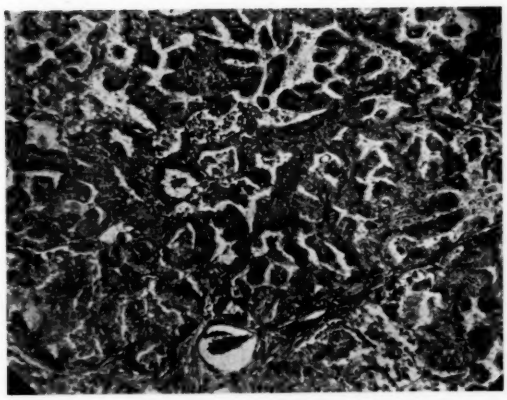

FIG. 3.
Single layers of proliferating epithelium in a grossly affected area.

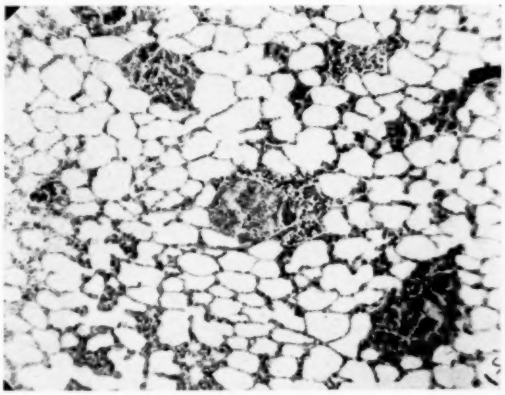

FIG. 2.
Discrete foci of epithelial proliferation in a lightly affected area.

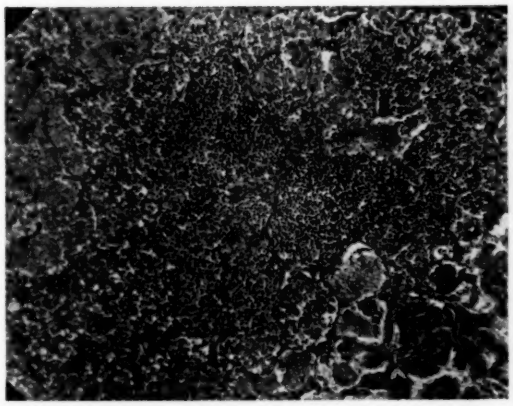

FIG. 4.
Areas of epithelial proliferation surrounded by alveoli showing various types of cellular reaction.

proportion of the apparently normal South African sheep which he examined.

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PRODUCTION OF FEEDING-STUFFS IN GREAT BRITAIN

Supplementing his study of Britain's supplies of feeding-stuffs from all sources (see *Nature*, September 14th, p. 362), Dr. Norman Wright has investigated quantitatively the problem of making good war-time deficiencies by using new sources of indigenous materials and by improved conservation of all supplies (*Agric. Prog.*, 17, Pt. 2). He finds that conservation of all slaughter-house offals would only just offset the greatly diminished supplies of fish-meal, and that large-scale utilisation of kitchen waste would provide a mere fraction of our requirements. Of greater significance is the officially projected production of one million tons of grass silage, but this amount would involve the construction of about 30,000 silos, each of 30-35 tons capacity; and if 10 per cent. of the straw not used for stock-feeding were converted into a digestible cellulosic feed by predigestion with alkali, more than 20,000 digestion tanks and about 22,000 tons of caustic soda would be required.

Neither the direct use of urea or ammonium bicarbonate to make good the protein deficiency in cereal and other starchy foods, nor the doubling of the existing acreage under beans, would appreciably add to our resources in protein materials. More hopeful would be the economising of imported feeding-stuffs by adopting the Lehmann system of pig-feeding (restricting the cereal meals and using more boiled roots, potatoes, etc.); the reduction in the protein ration of dairy cows from 0·6 lb. to 0·5 lb. protein equivalent per gallon of milk; and by putting all poultry on minimum feeding allowances. These savings would represent about three times those to be secured from possible new sources of supply. The total savings from all sources would represent 11·7 per cent. protein equivalent and 8·9 per cent. starch equivalent of our pre-war home production, but only 8·5 and 6·9 per cent., respectively, of out total pre-war supplies.—*Nature.*

* * * * *

The Wellcome Foundation Ltd.—Mr. George E. Pearson has retired from the Board of The Wellcome Foundation Ltd., of which Mr. T. R. G. Bennett has been elected Chairman and Mr. G. L. Moore Deputy-Chairman. Dr. R. A. O'Brien, who joined the staff of the Wellcome Physiological Research Laboratories at Beckenham in 1910 and became Director in 1914, retired at the end of 1940. Dr. J. W. Trevan, who became Head of the Pharmacological Section in 1920, has been appointed to succeed him.

* * * * *

At a meeting of the Small Pig Keepers' Council held in London and attended by representatives of a variety of agricultural interests, the Chairman, Mr. Cedric Drewe, M.P., reported that the number of registered pig clubs now exceeds 300, and that they continue to increase steadily. This represents over 10,000 cwt. of additional pig meat being produced in a year, mostly from edible waste, much of which might have been destroyed.

Roaring and Whistling in Thoroughbred Horses*

BEN. RUNCIMAN, M.R.C.V.S.
JOHANNESBURG

An article in the December number of the *Journal of the South African V.M.A.* prompts me to write this. Some time ago I brought a proposal before the S.A.V.M.A. about the importation of unsound horses into this country. This proposal, after some opposition, was carried, but although it was intended for the Government I cannot find that it reached this destination, although the Government derives a substantial sum per annum from the tax on imported racehorses. This tax applies only to horses imported for racing, those for breeding come in tax free. The man who imports and pays tax wants to win races and, therefore, makes some provision to see that the animals are sound. The breeder who imports duty free, brings in any unsound animal, because, as Drs. Quinlan and Steyn remark, they can be obtained at a much reduced price.

Sound animals to race; unsound ones to breed from, what a noble effort to improve the breed of horses in this country!

Dr. Quinlan states that roaring is not increasing in South Africa and that it is probably not hereditary. I have had nearly 40 years' experience with thoroughbreds both in this country and in England, and I feel I cannot let that statement go unchallenged. Roaring is on the increase. Thirty years ago I knew of only one South African bred horse a roarer and this was a galloway named "Elphinstone" sired by a bad roarer. To-day we can find them on any racecourse; 14 have been treated at Onderstepoort, but this does not comprise all the roarers in all our centres. The increase in the number of roarers was very apparent to me when I returned to this country in 1933, after ten years' absence. It is true that more horses are being bred, but the roarers are out of proportion to the number bred.

At one time it was thought that one could not breed roarers in South Africa. Since the influx of roaring sires we have bred them, and plenty of them. During the last 20 years 50 per cent. of the stallions imported have been wrong in their wind. May I ask why we should import unsound animals, no matter what their breeding and turf performances, when sound animals can be obtained? It is a question affecting the whole horse breeding industry of the country and not merely the breeders' pockets. The breeders, to quote from the article in the *Journal of the S.A.V.M.A.*, were forced "to take a chance." A chance of what? Filling the country with unsound horses?

It is, however, pleasing that there are still some breeders who will not have a roarer, and we have NON-roarers just as well-bred and performed as the roarers, but not, of course, bought at a roaring price, which in many cases is what one likes to offer, for roarers have no value in the country of their origin and no other country wants them.

The following horses developed roaring without any previous illness: "Floros," "Herne Bay," "Stormont," "Prunus," all sons of "Kerasos" (roarer); "On the Square," son of "Rampart" (roarer). These horses, according to the information given to me by their trainers, "just turned roarers," some at three, some at four, and some at five years. These are all Johannesburg-trained

*Contributed to the September, 1940, issue of the *Journal of the South African Veterinary Medical Association* (**11.** 113-116.)

horses. What other centres of racing have experienced I do not know. "Ponell," when he won the Natal Derby and Guineas, was a whistler and his wind got worse. He won races after his operation. "Stormont" won the S.A. Derby on an objection, *then* sound in his wind; subsequently, for no apparent reason, he developed roaring. He was operated on, put into training, but turned out useless. "Waterproof" became useless for racing and was given away as a hack.

The examples given of the four sons of the roaring "Kerasos," all roaring for no apparent reason, will surely give supporters of the non-hereditary viewpoint some food for thought. There was no history of previous illness; then why did they roar, if their roaring sires had nothing to do with it? I can only come to one conclusion —they inherited it from one or perhaps from both parents. I will readily admit that after strangles and biliary fever some, but not all, horses roar. Those with roaring ancestors are invariably the sufferers, and the roaring ancestor may be two generations back. Roaring stallions in some cases have not produced many roarers, but their sons whose wind was sound have been roarer producers. Those who deny the hereditability of roaring are forever quoting the roaring mare "Pocahontas" who produced "Stockwell" to bolster up their theory. If they had troubled to look a little deeper into the stud record of "Pocahontas" they would have found that her first foal, a colt by "Camel," was a roarer. A glimpse into the attitude of some countries (and these countries breed good horses) to roaring stallions may be of interest. In February, 1939, a conference was held in the Agricultural Hall, Islington, to discuss various statements which had appeared in the Press stating that roaring was not a hereditary disease. Dr. Adair Dighton, F.R.C.V.S., said it was non-hereditary. The President of the Clydesdale Horse Society said, "Roaring in horses is hereditary and they should not be bred from." One may assume this gentleman had some experience of horse breeding to make so definite a statement.

Lord Rosebery, President of the Thoroughbred Breeders Association, said, "From my study of the pedigree of horses, I agree with the opinion of the National Veterinary Medical Association that roaring is hereditary." This from a man, a keen student of breeding, who bred a Derby winner. Dr. Bullock, Secretary, Royal College of Veterinary Surgeons, "I beg to inform you that in 1888 this College was asked to supply information as to what were considered to be hereditary diseases of horses to the Royal Commission on Horse Breeding. Circulars were issued to all veterinary surgeons and the replies tabulated. As a result it was found that there was a consensus of opinion that roaring must be classified as a hereditary disease. The rules as to the licensing of stallions in France also provide that a stallion suffering from chronic roaring is not eligible for a licence. This was settled by the law of August 14th, 1885, supplemented by the law of March 8th, 1923. Stallions are not bought by the State Stud Administration if they suffer from chronic roaring, and if a stallion belonging to the stud becomes a roarer he is either castrated or destroyed."

Very good for France. I might mention that tubed horses are not allowed to compete in races in France. I cannot say whether this rule also applies to horses operated on for roaring.

Mr. J. B. Robertson, M.R.C.V.S., "Mankato" of the *Sporting Chronicle*, one of the greatest authorities on Thoroughbred horse breeding in the world, said: "I have noticed in the Press recently certain irresponsible and illogical expressions of opinion that roaring in horses is not hereditary. Not one of the writers observes the first principle in the grammar of genetics, namely, whether or not the incidence of roarers and whistlers is larger in the descendants of roarers and whistlers than in the offspring of horses and mares not affected with the lesion, or in the cases of horses in general. After collecting data for over 60 years in the case of Thoroughbreds and examining hundreds of horses and mares from the hereditary aspect in Thoroughbreds and also very many horses for the Ministry of Agriculture under the Horse Breeding Act of 1919, the evidence at my command is overwhelming that paralytic roaring and whistling are due to hereditary factors. . . . There is no better illustration than 'Lily Agnes' (roarer), her son 'Ormonde' (roarer), his son 'Goldfinch' (roarer), his daughter 'Chelandry' (roarer)." [Mr. Robertson could have added "Chelandry's" son "Traquair" (roarer)]. Mr. Robertson goes on to say, "I doubt if those who claim that roaring is purely an acquired defect know anything about the ancestry and history of roaring Thoroughbreds. I have not noticed that they advance any statistical data in support of their pathological and Weismann theories."

There would have been more interest, from the hereditary point of view, in the list of animals operated on at Onderstepoort, if suggestions had been made as to why these animals roared, *e.g.*, strangles, biliary fever, roaring parents. We are told so many horses roared, and that roaring is not hereditary. I want a much more convincing statement before I follow the Onderstepoort authorities.

Some of the horses operated on are got by roarers, and others have roaring strains on the dam's side. I should, however, like the non-believers in the hereditability theory to explain why "Boy Cherry" roared. He was by "Rampart" (roarer), out of "Cherry Red" and own sister to the roaring "Camelot" also operated upon at Onderstepoort. "Cherry Red" and "Camelot" were both by "Kerasos" (roarer). This is in-breeding to roarers with a vengeance.

In Tattersall's sale catalogue is the following: "Caffyns" by "Coronach" out of "Buck Barn" (Hobdayed), "Pike Barn" by "Papyrus" out of "Buck Barn" (Hobdayed) ("Hobdayed" is another term for the operation for roaring). These horses are by different sires but out of the same dam and they may have inherited roaring from "Buck Barn," a daughter of "Buchan," who has a roaring son at stud in this country.

I await with anxiety an explanation of why "Boy Cherry," "On the Square," both sons of the roaring "Rampart," and also why "Floros," "Herne Bay," "Stormont," "Prunus," four sons of the roaring "Kerasos," were all roarers.

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CLINICAL COMMUNICATION

A Case of Metrocele and Mastitis in a Bitch

L. GUY ANDERSON, M.R.C.V.S., B.V.SC. (Tor.)
AYLESBURY

Subject.—An eight-year-old Dachshund bitch.

History.—The patient was first seen in May with enlarged inguinal mammary glands. A diagnosis of mastitis (probably streptococcal) was made, the condition following pseudo-pregnancy, and suitable treatment resulted in an apparent cure. The bitch was next seen in October of this year. There was a large swelling in the inguinal region, and a history of having been accidentally covered about six weeks previously. Metrocele was diagnosed and an operation decided upon.

Operation.—Intravenous nembutal anaesthesia was used, and the site prepared in the usual way. The skin incision was almost longitudinal on the lateral surface of the mammary gland.

On opening the herniated inguinal sac, it was found that both horns of a gravid uterus had descended through the canal. The uterus was removed by the usual surgical procedure, the ring closed with catgut and the skin with silkworm gut.

The patient made satisfactory progress for three days, but on the fourth day the inguinal region was terribly swollen, the bitch very weak with a temperature of 103 deg., and an almost imperceptible pulse. A tentative diagnosis of a strangulated bowel hernia was made and the patient prepared for a second operation. At this stage a very grave prognosis was given as the animal was aged, had not recovered from the shock of the first operation, and was so weak and toxic that it was impossible to raise a vein for injection.

A small dose of nembutal was given intraperitoneally, and anaesthesia completed with chloroform and ether. On removing the sutures from the first incision and examining the region, it was found that the swelling was due to a very acute mastitis which was causing septicaemia. It was decided completely to excise the two posterior glands on that side. This entailed a tremendous incision, but it was felt that the removal of the focus of infection was the only way of saving the animal's life.

After the operation a large dose of prontosil was given intramuscularly and coramine and glucose-saline hypodermically. With careful nursing the animal made an uninterrupted recovery.

DISCUSSION.—There were two points of particular interest in the case. Firstly, that both horns of the uterus were found in the hernia. This is, I believe, most unusual. Secondly, it was an interesting example of how destruction of tissue, or at least injury to tissue, rather than the mere presence of bacteria, seems to be the main factor in infections following wounds. It would appear that, very often, the actual presence of pathogenic bacteria causes little or no trouble, until the natural defences of the tissues are weakened by trauma.

ABSTRACTS

[PASTEURISATION OF MILK: SOME RECENT ASPECTS. KAY, H. D. (1939.) *Nutrit. Abstr.* **9.** 1-11.]

More hygienic methods of milk production and distribution have to some extent decreased the need for pasteurisation as an aid to the keeping quality of milk, but, since bulked milk almost always contains milk from diseased udders, some efficient form of heat treatment is needed in the interests of public health. The effect of pasteurisation by the " holder " process on the nutritive value of the milk is discussed, and much of the earlier work on this subject is adversely criticised on the grounds of faulty design of experiments. Feeding trials under comparable conditions show that for calves and for rats, any difference between raw and pasteurised milk is negligible. Observations on children under the " Milk in Schools " scheme also gave no evidence of difference. From such chemical and physical studies as have been made, the total change following on holder pasteurisation is summarised as " a 20 to 25 per cent. loss of vitamin B_1, a loss (not entirely due to the process) of 20 per cent. of the vitamin C, and a possible loss of 20 per cent. of the small iodine content of the milk." Seasonal changes are responsible for greater changes in the nutritive quality of the milk than pasteurisation.

" Sterilisation " of milk (heating to 212° F.) results in greater injury to the nutritive quality than the holder process. The biological value of the proteins is, in this case, lowered by about 6 per cent.

Observations in areas where milk is pasteurised by the holder process have shown that a surprisingly high percentage (up to 40 per cent. in some cases) of the product has not been effectively treated. This failure is probably due to lack of the necessary care in operation of the plant, and to the difficulty of controlling the temperature of the large volume of milk for the long period. Kay draws attention to the possible advantages of the high-temperature short-time process. Improvements in the design of the plant used for this technique have obviated many of the defects of older types, such as irregularity in temperature, and the ease of control of the process compares well with the holder process. Mattick and Hiscox have studied the conditions necessary for efficient pasteurisation by the high-temperature short-time process, and conclude that a machine run at 162° F. with a holding of the milk at this temperature for 15 seconds, is satisfactory, giving a good margin of safety in killing tubercle bacilli, and interfering little with the commercial value of the milk. The phosphatase test is as reliable a check on the efficiency of pasteurisation by the H.T.S.T. process as by the holder process. 0·2 per cent. raw milk added to pasteurised milk is detectable by this test, and it is of great importance in the control of pasteurisation.

J. B. B.

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[LATENT VIRUS INFECTIONS AND THEIR POSSIBLE RELEVANCE TO THE CANCER PROBLEM. ANDREWES, C. H. (1939.) *Proc. Roy. Soc. Med.* **33.** 75.]

There are many viruses which are known to cause latent infections. Thus, yellow fever, influenza, and poliomyelitis viruses may all cause transient subclinical infections in man, the evidence of such latent infection being derived from the appearance of anti-

bodies in the blood. The psittacosis virus is usually demonstrable in the livers of young healthy budgerigars in Californian aviaries, and the viruses of equine infectious anaemia, fowl-pox, and laryngo-tracheitis, may persist within their hosts long after symptoms of the disease have disappeared. It is believed that man may in the same way harbour the Herpes virus in some unknown situation in the body for antibodies are known to persist in the blood of adults after an attack of herpetic stomatitis in early childhood, and such adults are prone to local herpes eruptions when a suitable provoking stimulus, such as a cold or fever, occurs.

There are certain strains of laboratory mice which remain permanently infected with the chorio-meningitis virus which is passed from generation to generation *in utero*. No symptoms are displayed, and the virus can only be demonstrated by inoculating tissue extracts into a strain of mice which is not immune to the virus. Analogous indigenous virus infections are seen in many plants—for example, certain strains of potato—which may harbour a virus the presence of which is only demonstrable by the inoculation of other plants susceptible to it, or by disturbing the virus-host equilibrium by growing the infected plant in a certain environment. It is also well known that certain bacteria are indigenously infected with phages which can only be indicated by the action of their filtrates against other bacteria.

Many other examples are quoted and attention is drawn to the similarity to these latent virus infections of certain facts in experimental cancer research. The fact that most normal fowls develop neutralising antibodies against filtrates of the Rous sarcoma virus suggests that they may carry or have had contact with a virus serologically related to it. It is known that by the intramuscular inoculation of tar the development of sarcomata transmissible by filtrates may be induced in such fowls and this suggests that an indigenous infection has been activated by a disturbance of the cell-virus equilibrium. Tar is similarly known to stimulate the growth of tumours in rabbits infected with the Shope's infectious fibroma and papilloma viruses. Evidence is also accumulating to suggest that fowl paralysis, which has many neoplastic characteristics, is the chronic stage of a symptomless infection probably caused by a virus.

Experimental evidence suggests that the embryonated ova of lung-worms passed in the faeces of a pig infected with swine influenza may carry the virus throughout their life-cycle in the earthworm and back to the lungs of a susceptible pig, where the virus remains dormant within the worms until some provoking stimulus—such as infection with *H. influenzae suis*—lights up the infection and causes the pig to develop overt symptoms of influenza. The virus has not yet been demonstrated in the infected lungworms, but it is possibly present in some altered form. Other infections are known (non-filterable sarcomata of fowls; rabbit papillomata) in which the virus can only be demonstrated by roundabout means, and it is possible that such viruses may have lost some aggressive component, which may be likened to teeth, due to disuse atrophy—a factor which would become prominent in the case of neoplasms, where virus could be handed on from cell to cell during cell division and the need to come out of the cell to seek normal cells would disappear. The demonstration of such "toothless" viruses may therefore be very difficult and it is possible that the long immunity induced by many virus infections may be due to such a modified virus persisting within the host. H. H. S.

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[EFFECT OF PHENOTHIAZINE ON THE DEVELOPMENT OF ROUNDWORM LARVAE IN THE FAECES. Shorb, D. A., and Habermann, R. T. (1940.) *Vet. Med.* **35**. 454-457.]

The successful use of phenothiazine as an anthelmintic, reported in scientific literature by various research workers, has suggested to Shorb and Habermann that, if given in small doses either in capsules or mixed with the food, this chemical might have a deleterious effect on the development of nematode larvae. To test this suggestion, the authors carried out a number of experiments on sheep naturally infected with roundworms. Details of the experiments and of the materials and methods used are given. It was found that when 7 gm. phenothiazine were administered, in gelatin capsules, daily for three days the number of larvae developing in 50 gm. faecal cultures dropped from about 123,000 to 16,560 on the day following the first dose. Although cultures were negative on the succeeding three days, larvae re-appeared in the cultures made on the third day after the last dose and increased markedly on the fourth day. There was, however, some anthelmintic effect on the adult worms because the egg counts did not regain their numbers prior to treatment. When administered to sheep at the rate of 0·25 gm. per day in the food it failed to inhibit larval development but at the rate of 0·5 gm. per day for seven and nine days inhibition of larval development, except in the case of *Strongyloides papillosus*, was observed in cultures of faeces passed 48 hours after the administration of the first dose and continued for 48 hours after the last dose had been given. When thoroughly mixed with sheep faeces containing *Haemonchus contortus* eggs only, phenothiazine, at the rate of 1 per cent. by weight, inhibited the development of all larvae; in amounts of less than 1 per cent. larval development was retarded. J. N. O.

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[EXPERIMENTAL PRODUCTION OF DIGESTIVE TRACT ULCERATIONS. Penner, A., and Bernheim, Alice I. (1939.) *J. exp. Med.* **70**. 453-460. (1 table, 7 figs. on 2 plates, 11 refs.).]

These experiments were undertaken in an attempt to reproduce in dogs certain ulcerative lesions which had been found at autopsy of human subjects and which were considered to have arisen as the result of the compensatory vascular phenomena occurring in shock. The method adopted was the causation of a prolonged sympathetic stimulation of the vascular bed through the intraperitoneal injection of adrenaline, which was administered to different animals over periods of from five to ten days at a maximum dosage of 0·3 to 0·5 mg. per kg. After each injection a "rage reaction" was noted in some animals, and restlessnesses, tachycardia and cyanosis in others. At the end of the experimental period the dogs were destroyed and autopsied, with the following general findings. The antrum of the stomach appeared pale, but the fundus and body were congested, and there was a mottled congestion of the duodenum. In the jejuno-ileum the congestion increased from the proximal end to the distal, in which portion there were both small mucosal ulcers and larger ulcers extending to the submucosa. The bases of these ulcers, which were generally confined to the anti-mesenteric portion of the bowel, were haemorrhagic

and sometimes covered with a greenish, diphtheritic pseudomembrane. The length of intestine affected varied from 9 cms. to 50 cms, but lesions did not occur within at least 6 cms. of the ileocaecal valve. There was no evidence of peritonitis. Renal lesions occurred, but their nature is not fully described.

[These findings have been given in detail in order that practitioners may compare them with the so-called "haemorrhagic gastro-enteritis" of greyhounds and other breeds. The *post-mortem* findings of this disease have been said to resemble those of shock.]

A comparison of the results obtained in dogs with those seen in man indicated that while the canine lesions appeared to originate in the mucosa, the human lesions developed from the submucosa. This is explained by reference to the work of Spanner (*Jahrb. Morph. u. Mikr. Anat.*, 1932. **69.** 394) who noted important species differences in the vascular supply of the intestinal wall. Thus in man, certain rodents and the bat, the main arteriole supplying a given villus is said to pass up to the villar tip before dividing into two branches, one of which passes directly into the main venous channel of the villus and so forms an arteriovenous shunt. In the dog, cat, pig and horse, however, the anastomoses occur in the submucosa: in these species, therefore, vasoconstriction of the arteriole beyond the shunting point would lead to a cessation of blood to the mucosal area and so pave the way for the formation of localised necrotic lesions such as were found in the present experiments.

A confirmation of these views was obtained by the present authors, who repeated the adrenaline experiments on three other species. In the rabbit and guinea-pig the changes resembled those in man, whereas in the cat the lesions were again mucosal in origin. A. N. W.

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[COMPLEMENT-FIXATION TEST WITH TISSUE CULTURE ANTIGENS AS AID IN RECOGNISING LATENT AVIAN PSITTACOSIS (ORNITHOSIS). MEYER, K. F., EDDIE, B., YANAMURA, H. (1939.) *Proc. Soc. Exp. Med. Biol.* **41.** 173-176. (1 table, 4 refs.).]

Until recently it has been the policy of the U.S. Department of Agriculture to destroy all birds of shipments in which any case of psittacosis has occurred. Valuable and rare birds which have proved to be free from disease on autopsy have thus been needlessly destroyed. Experiments conducted on a shipment of Australian parrots have indicated that the complement-fixation test may detect carrier birds with a high degree of accuracy and thus obviate the necessity of unnecessary destructions.

The test is similar to that used for the diagnosis of human psittacosis. As antigen, concentrated trypsin-digested cultures of the psittacosis virus in Rivers-Li media are employed. Serum is obtained by bleeding the parrots from the ulnar vein while under ether anaesthesia.

The accuracy of the method was tested on 45 Australian cockatoos and parrots. Fourteen of the birds died during a period of two weeks' quarantine in California. Ten proved to be infected with psittacosis. The remaining 31 birds were subjected to the complement-fixation test and then autopsied. In every case birds with a latent infection of the disease reacted to the test. In a few cases non-infected birds reacted. These subjects probably possessed a sterile immunity. D. D. O.

REVIEW

The Science of Animal Breeding

Under the above heading, *Nature* (**146**. 668) publishes the following review, by Dr. H. P. Donald, of "Animal Breeding," by Prof. Laurence M. Winters. [Third edition. Pp. viii+316. (New York: John Willey and Sons, Inc.; London: Chapman and Hall, Ltd., 1940.) 21s. net.]

Animal breeding, says Professor Winters, is the art of improving animals. As such, it depends for success on a skill of hand and eye which can scarcely be acquired from books, and indeed, in this third edition of his book, Professor Winters is not so much concerned with the art as with giving students an up-to-date account of the science. His pages offer the younger generation of breeders and extension workers the gift of science to animal breeding—the organised knowledge which enlarges the scope and power of the enterprising craftsman. That the author now addresses himself to students involves an interesting transition, since the progressive breeder for whom the first edition was written has been deserted for the student whose background of fundamental sciences renders many modern investigations more intelligible.

Beginning with historical glimpses of the development of domestic animals, the book continues with the anatomy of the genitalia, the physiology of the breeding cycle, the cytology of the gonads, and the technique of artificial insemination. Following this selection of applied sciences and at greater length is an exposition of inheritance which follows orthodox lines. Mendel's laws are explained and illustrated with some well-known simple examples, and then the more complicated genetic situations presented by selection and breeding for economic characters are considered. The choice of the most significant items from an enormous mass of literature is difficult, and it is scarcely to be expected that any two authors would agree on the way to do it. Experienced readers may therefore think that some subjects in which they are interested, such as adaptation to environment, the creation of new breeds, or progeny testing, have received too little attention for a text-book, and that others, such as selection and breeding systems, have not been considered sufficiently from the point of view of the breeder whose difficulties will ultimately have to be met by the student. The author's wide range of experimental studies with their practical background well qualifies him as a guide for students, so that it seems a pity he has not dealt more fully with improvement as the breeder sees it.

To enunciate a number of good scientific reasons for following a certain line of action is one thing; to decide which of the multifarious and often conflicting considerations that arise in practice should receive greatest weight is quite another; and ignorance of the latter often breeds distrust of the former. Another feature that might be criticised is the use of illustrations from the 1924 edition, for example, Figs. 69 and 117, which are rather poor by 1940 standards. Whatever may be said of the details of his treatment, no one can complain that Professor Winters is satisfied with the present rate of improvement in livestock. He wants shows to be occasions for instruction rather than carnivals; record of performance tests made and used; artificial insemination, cross-breeding and

(Concluded at foot of col. 1, page 42.)

NOTES AND NEWS

The Editor will be glad to receive items of professional interest for inclusion in these columns.

Diary of Events

Feb. 6th.—Central Veterinary Society: Council Meeting 11 a.m.; Annual General Meeting 12 noon; Ordinary General Meeting 2 p.m.—all at the Palmer Hall, West Street, Reading.

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The Survey Committee

Negotiations for the implementing of the Association's policy as at present outlined in the First Report of the Survey Committee are actively proceeding. Already two long conferences have been held at the offices of the Agricultural Research Council between representatives of the Animal Health Division, the Agricultural Research Council and the National Veterinary Medical Association. At the first meeting, held on December 20th, at which Mr. D. A. E. Cabot, Chief Veterinary Officer to the Ministry of Agriculture, occupied the Chair, the subject of mastitis was discussed. The second meeting was held on January 10th, when, owing to the indisposition of the Chief Veterinary Officer, the Chair was taken by Mr. E. C. Lloyd. At this meeting contagious bovine abortion, sterility and Johne's disease were considered.

Full discussion ensued at both of the meetings and it was encouraging to note that a large measure of agreement was attained. As a result of these conferences, certain advice is being tendered to the Ministry of Agriculture which it is hoped will facilitate the inauguration of the campaign put forward by the N.V.M.A.

At one or both of these meetings the following represented, all were called by, the bodies named: the Agricultural Research Council—Sir Joseph Arkwright, Sir Joseph Barcroft, Sir Merrik Burrell, Professor T. Dalling, Mr. E. Fleming, Dr. J. Hammond, Dr. A. T. R. Mattick, Sir Thomas Middleton, Mr. S. E. Rusk, Dr. A. W. Stableforth, Professor W. W. C. Topley and Mr. E. H. E. Havelock (Secretary). The Ministry of Agriculture was represented by Dr. W. H. Andrews, in addition to Mr. Cabot and Mr. Lloyd, while the Ministry of Health was also represented by Sir Weldon Dalrymple-Champneys and Dr. W. E. Lethem. The representatives of the Association were the President (Mr. H. W. Steele-Bodger), Dr. W. R. Wooldridge, Professor Wm. C. Miller, Mr. G. N. Gould, Mr. S. L. Hignett and Dr. A. D. McEwen.

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PERSONAL

Colonial Veterinary Service Appointments.—The following first appointments to the Colonial Veterinary Service are announced: Messrs. G. L. Bannister, M.R.C.V.S., Veterinary Officer, Tanganyika Territory; J. D. Birkett, M.R.C.V.S., Veterinary Officer, Nigeria; R. W. E. Lewis, M.R.C.V.S., Veterinary Officer, Kenya, and I. B. Pullon, M.R.C.V.S., Veterinary Officer, Tanganyika Territory.

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R.C.V.S. OBITUARY

Purvis, George Burnett, 21, Park Road, Grahamstown, C.P., South Africa. Graduated Edinburgh, July 7th, 1920; Fellowship July 26th, 1926. Died November 24th, 1940.

heterosis exploited. In short, he wants progress to be hastened by all available methods, a desire which all his readers will share.

The Late Mr. G. B. Purvis, F.R.C.V.S.

We record with much regret the death of Mr. George Burnett Purvis, F.R.C.V.S., which took place at his home in Grahamstown, South Africa, after an illness, lasting over seven years, and which he bore with the utmost fortitude.

Soon after qualifying Mr. Purvis was appointed to the Kenya Veterinary Service and, after a short period in Africa, to the Malayan Veterinary Service. In Malaya he became very interested in helminth parasites and made collections of parasites of that part of the world, publishing papers on these studies. He was also much interested in East Coast fever.

A few years ago Mr. Purvis contracted tuberculosis and became seriously ill. As a result he was compelled to leave Malaya and seek a climate more suitable for his constitution. The sympathies of Mr. Purvis's colleagues go out to his widow, while we mourn the loss of a useful and enthusiastic member of the profession whose career has thus sadly been cut short.

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RATIONED FEEDING-STUFFS FOR HORSES

Owners of urban horses are urgently reminded by the Ministry of Food that after February 1st supplies of feeding-stuffs (including oats, beans, and bran) will be obtainable only by means of official ration cards or coupons. In order to get ration cards and coupons owners must register their horses at once; forms are obtainable at any local food office.

The registration scheme applies to all urban horses, including mules, asses, jennets and donkeys. It does not apply to horses already registered with county war-agriculture executive committees or agricultural departments; horses and ponies employed in the mining industry; Army horses and mules; and horses in racing and hunt stables.

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"HOW DO DRUGS ACT?"*

(*Continued from page* 33.)

Exemplifying "the second way in which drugs may act: by modifying the chemical changes within the cell itself," Sir Walter Langdon-Brown said that, although he had stated that vitamins provided the best illustration of this, he should start by discussing some of the activities of thyroid extract, since this is so widely used therapeutically. "Its quickening effect on metabolism has been described as the draught to the fire. Note that it speeds up metabolism in the direction it is normally going. Thus, if a little thyroid extract is added to water containing some tadpoles they quickly metamorphose into tiny frogs. Now in that change the gills shrink to nothing and the limbs begin to grow, and it is possible to see under the same field of the microscope the cells of the gills rapidly breaking down and the cells that are going to form the front legs multiplying with equal rapidity under the influence of thyroid.

"Thyroxine, the active principle of the gland, is the only animal substance that contains any notable amount of iodine. Our marine ancestors obtained their iodine from sea water, and their rudimentary thyroids were placed close to the gills so as to fix that iodine. The first effect of iodine shortage is thyroid enlargement. The gland 'gasps' for it. Giving iodine helps it to return to a more resting state. It is curious that this should also help in hyperthyroidism, as it undoubtedly does. You can apparently saturate the thyroid of exophthalmic goitre with iodine in a fortnight, and it will remain saturated for about six weeks.

"From the obvious effects of iodine on the thyroid it has been claimed that the therapeutic effect of iodine or iodides is entirely due to their altering the state of

*Address by Sir Walter Langdon-Brown to the Pharmaceutical Society (*Pharm. J.*, February 17th and 24th, 1940).

activity of the thyroid gland. This is probably too narrow an interpretation; note the purely chemical influence of iodide in rendering a metallic compound more soluble, and thus eliminating it more readily from the system—for example, mercury and lead, or toxins such as that of syphilis. May it not act in the same way in removing less recognised toxic substances? Thus iodide does not lower normal blood pressure, but does lower raised blood pressure. Is it by elimination of pressor amines absorbed from the bowel?

One thing about thyroxine is quite certain—that it causes the consumption of more oxygen because of the increased rate of combustion. This leads me to the question of the influence of drugs on oxidation within the cell. Why do you remain out of breath for some time after violent exertion? Because you have incurred what has been called an oxygen debt, which has to be repaid by inspiring increased amounts of air afterwards. Sugar is the fuel used by the muscles, and if this is not completely oxidised some of it remains in the circulation as lactic acid, which irritates the respiratory centre to increased activity. Since the burning of a piece of sugar is a simple matter, one might suppose that to oxidise it within the body would also be simple. But the body has to carry out the process without alterations of temperature, osmotic pressure, etc., which renders it a highly complicated procedure. A whole series of enzymes are required, and a very interesting fact has recently been discovered, namely, that vitamin B_1 is an essential partner in this series. The more sugar, or starch, which becomes sugar, that we eat the more vitamin B_1 we need to oxidise it. But there is another thing which needs this vitamin to oxidise it, and which is sometimes unfortunately taken in excessive amounts, and that is alcohol. It has recently been discovered that alcoholic neuritis can be greatly alleviated by large doses of vitamin B_1, even though the patient continues to drink. The neuritis is not due to the alcohol itself, but to the alcohol capturing the vitamin before it can get to the nervous system, where it is needed if the nerve cells are to utilise their oxygen. Alcoholic neuritis is, therefore, a deficiency disease in exactly the same way as beri-beri is due to eating polished rice and thereby taking a lot of starch without the compensating vitamin. Clearly oxidation within the cell cannot proceed without both sugar and vitamin B_1. . . . Oxidation of sugar is necessary not only for the brain but also for the muscles. When our voluntary muscles are diseased or fatigued we rest them. But there is one muscle that can never rest, and that is the heart. Therefore its need of vitamin B_1 is more urgent.

The Body's Need of Iron

"That iron plays an important part in oxidation has long been known. Its tendency to rust, which is one of its disadvantages in industry, is its great physiological merit, for by its alternate oxidation and reduction in haemoglobin oxygen is carried all over the body. We have now learned in addition that ferrous iron contains one more electron than the ferric, and that the handing over of this electron is the activator of the series of oxidative changes in the cell to which I have already referred. We have also learned the exact stage in the manufacture of red blood corpuscles that iron is required.

"Now our daily requirement of iron is only about 3 grains, less than is contained in any ordinary good mixed diet. Yet we know that 90 grains of iron and ammonium citrate a day are required for the cure of ordinary anaemia, and even though 6 grains of ferrous sulphate a day are sufficient, that is double the physiological demand. It seems that in disease it is sometimes necessary to 'swamp' the body with a drug before it can produce its effect, as if there were some obstacle to its absorption which has to be overcome by mass action. Probably one such obstacle in the case of iron is the absence of hydrochloric acid in the gastric juice which is so common in anaemias, but I doubt whether this is the whole story. Certainly the iron salts are more soluble in its presence, but that argument does not apply to all the instances in which mineral salts have to be given in large doses to meet a comparatively small demand by the body. Other factors come in; thus we know that vitamin D is necessary for the absorption of calcium from the bowel and parathormone from the parathyroids is required to keep an adequate quantity of it in the circulation; also that sodium cannot be sufficiently retained in the body in the absence of adrenal cortical secretion. It has also been maintained that thyroid secretion is needed before iron can be built up into haemoglobin. So it would appear that hormones and vitamins play an important part in enabling mineral salts to produce their proper effect on the tissues, but that when they are deficient, absorption and utilisation can sometimes be forced on the body by mass reaction. Nevertheless it is obviously more physiological to assist our mineral drugs by the appropriate hormone or vitamin if we know what it is.

The Tale of Ascorbic Acid

"This is perhaps a departure from my main thesis concerning drugs and oxidative processes. Although the story of vitamin C (ascorbic acid) is now a twice-told tale I feel justified in referring to it because it is now so widely used as a drug and because as a strongly reducing substance it acts by balancing oxidation and reduction changes in the cell. We all know that lemon juice, and to a much less extent lime juice is an antidote to scurvy, and that it was found this was due to the vitamin C they contain. In 1924 the Hungarian biochemist, Szent-Györgyi, showed me the zone of strongly reducing substance he had discovered in the adrenal cortex. I asked him if he thought it was composed of vitamin C, to which he replied that this was what he was trying to find out. The difficulty was to prepare pure vitamin C. At the end of two years' work at Cambridge he succeeded in preparing 2 grams of it, and in determining its chemical structure. On his return to his native land it occurred to him to try to extract it from paprika, the Hungarian red pepper. At the end of one week's work he had got a whole pound of the pure vitamin. This recalled to my mind that historians tell us that some of the Elizabethan wars were to secure pepper fields. Peppercorns were regarded simply as food preservatives—but now it seems people had by accident stumbled against an important antiscorbutic. Presumably vitamin C is useful to the growing plant, for though it may be absent from seeds, it appears in the germinating shoot. Had this been known sooner many deaths from scurvy would have been avoided. In the laboratory it has been synthesised from a sugar, and as seeds contain starch a similar chain of events presumably occurs in nature. Unlike most other vitamins this one can be made by some animals—the dog for instance, who consequently never suffers from scurvy. It therefore behaves in some respects like a hormone. Much study has recently been directed to vague ill-health due to a lack of vitamin C, short of that necessary to induce scurvy. Our average requirement is 50 mgm. a day. If we take more than that the excess is excreted by the kidney; this gives a simple quantitative rule for determining the adequacy of a diet in this respect. If it is adequate and we add to it 50 mgm. of vitamin C we ought to be able to recover this amount from the urine; if it is inadequate some or all of this is retained by the body. Here then we have a clear-cut test for a dietetic deficiency responsible for vague ill-health, and the material ready to hand to re-establish healthy oxidation and reduction changes within the cell.

"Antitoxins and allied substances illustrate another way in which material usually of a protein nature can modify the chemical processes of the cell. I well remember the stir caused by the first experiments on the production of these protective antibodies, and it so happened that I was the clinical clerk of the first patient in this country to receive an injection of diphtheria antitoxin. We call the injected material an antigen because it provokes the cell to produce an antibody to it; if too much of a toxic anti-

gen is given straight off, the cell is overwhelmed, but if the process is repeated in carefully graduated doses these antibodies are formed in such abundance that they are set free in the blood, and the animal thus treated acquires an active immunity against that toxin. Moreover, the serum of that animal can confer passive immunity if injected into a patient suffering from that particular toxin. In 1907 Ehrlich produced a highly elaborate explanation of these phenomena: it is rather fashionable to-day to scoff at this explanation as being far too mechanical. But it should be remembered that his theory led him three years later to the production of Salvarsan and thus to the foundation of chemotherapy, which is now one of the most active developments in therapy.

"Chemotherapy also illustrates my third topic—the alteration of a drug by the cell so that it assumes fresh activity, yet with diminished toxicity. I had hoped that this lecture would have been preceded by one on chemotherapy by Dr. Leonard Colebrook, an expert on this subject. Unfortunately, he was unable to deliver it, but I can refer you to the admirable papers in our *Pharmaceutical Journal* for a clear exposition. I need, therefore, only touch upon it lightly here. Strictly speaking, the treatment of any malady with a chemical agent of known composition might be included in the term chemotherapy; actually, however, it is almost universally limited to the treatment of parasitic diseases by chemical disinfection or control of the causative agent without producing marked toxic effects in the patient. Now, just as vaccines apparently cause a reaction on living tissues leading to the formation of a new effective substance, so do some drugs—for instance, emetine in amoebic dysentery and arsphenamine in syphilis. Both of these are, however, ineffectve aganst the appropriate parasite in the test-tube. Therefore, the specific effect of such a drug depends upon its chemical interaction with some constituent of the living cell. It is necessary that the drug should be presented to the tissues in such a form as not to poison them. Thus arsenic in its inorganic form is highly poisonous; linked to a benzene ring compound, it can be tolerated by the patient in much larger doses, while the active arsenic is set free at the appropriate point; it appears to be changed by the cell from pentavalent to trivalent arsenic in the process.

How Sulphonamides Act

Chemotherapy has its disappointments, however; one such was optochin (ethylhydrocupreine). Although it has a powerful action in destroying pneumococci, which in the test-tube considerably exceeds that of the very successful M & B 693, it failed when put to the clinical test. Professor Henry Moore attributed this to two main causes—it cannot penetrate into the solidified pneumonic lesion, and it is so toxic that the safe dose is hardly effective. The most dramatic success of chemotherapy has been with the sulphonamides. They have the great advantage of being readily absorbed when given by the mouth. As Professor Fleming has recently pointed out, we have for the first time in the sulphonamide group, antiseptics which are more lethal to bacteria than to leucocytes. Sulphanilamide only interferes with leucocytes in concentrations 25 times greater than can be obtained therapeutically in the body, while it inhibits the growth of *Streptococcus pyogenes* in concentrations only 1/50 of such therapeutic concentrations. On the other hand it has little effect when large numbers of bacteria are present, and the presence of peptone interferes with its action. It is, therefore, unsuitable for local application, but highly suitable for action through the circulation. By paralysing the microbes in the circulation as it were it allows the natural defensive mechanisms to complete their destruction.

"It is a very interesting fact that just as the body can be educated by small doses of a toxin to resist larger doses, so a microbe can be educated by small doses of these drugs to resist larger doses of them. In the earlier days of Salvarsan treatment it was soon found that inadequate dosage made the spirochaete resistant to any further administration of arsenic. The same is true of sulphonamides. This I think proves that in chemotherapy a biochemical reaction is excited in the invading parasite.

"I should like to give another example of increased therapeutic and diminished toxic action resulting from the combination of a metallic drug with an organic vehicle, and that is mersalyl (Salyrgan), even though its action lies outside the rigid definition of chemotherapy. We know that in the kidney fluids are filtered out through the glomeruli, while the tubules concentrate the filtrate by re-absorbing much of the water. Now mercury particularly affects these re-absorbing tubules, and if a poisonous dose of, say, corrosive sublimate is taken they are gravely damaged. Yet if we give mersalyl, which, as we know, is an organic compound of mercury, their action is merely inhibited, so that concentration by re-absorption does not occur. For that reason mersalyl acts as a powerful diuretic by interfering with a normal process. In this way the mercury is rendered more therapeutic but less toxic. The pituitary gland apparently exerts some control over this re-absorption, and I have long suspected that in some cases of gross obesity associated with pituitary disorders the real cause of the increase of weight is retention of water or perhaps more accurately, increased re-absorption by the kidney tubules. This is confirmed by the dramatic reduction of weight which has followed the injection of 1 mil of mersalyl in this type of case. In two of my patients a single injection was followed by the loss of a stone in weight; in one of them this occurred within 12 hours. Of course, they put a good deal of it on again; curiously enough the one that lost weight most quickly regained it more slowly than the other, but in neither case was the original weight regained, and some of my patients have kept much better with an occasional repetition of the dose. Here the drug appears to override the antidiuretic effect of pituitary extract by simply diminishing re-absorption by the kidney tubules.

Chemical Structure and Physiological Action

"As the specific effect of a drug usually depends upon its chemical interaction with some constituent of the living cell, it was hoped that it might be possible to correlate physiological action and chemical constitution, but to a great extent the attempt has yielded disappointing results. In one instance, however, a definite relationship between physical state and physiological action has been made out. Certain hypnotics are relatively inert substances, and may differ widely chemically, but they have this in common, that they are soluble in fat and other lipoid compounds, and so tend to collect especially where such compounds exist—that is, the central nervous system, thus interfering with the normal working of the nerve cells. However, as Sir Gowland Hopkins pointed out, the investigation has been one-sided, and should involve consideration of the structure of the cell as well as that of the drug. A few years ago a striking instance of association between physiological action and chemical structure was demonstrated, largely through the work of Dodds. Oestrin, the ovarian hormone; vitamin D, *i.e.*, calciferol, which has such an influence on the orderly growth of bone; and the carcinogenetic substances to be found in tar, all contain the condensed carbon rings called phenanthrene. Thus it appears that normal reproductive activity, normal growth of bone, and that irregular, disorderly, unrestrained growth which constitutes malignancy are alike conditioned by this condensed ring, chemical alterations in it, apparently merely of hydrogenation, leading to extraordinarily different types of growth. The whole subject assumes fresh interest when we recall that phenanthrene was first derived from coal-tar and was, therefore, originally formed under the influence of sunlight ages ago, just as calciferol is formed in our own subcutaneous tissues by bright sunlight every summer.

"Dodds and Cook have carried out some strikingly interesting and important observations on the synthesis of sterols containing this phenanthrene ring as well as

of certain other hormones. Dodds found that simpler compounds than those prepared by the body can have the same effect as the natural hormones either to a less or even a greater extent. The basal group with the simplest chemical structure that can produce the biological effect he calls the 'skeleton key' which picks the physiological lock. Even more striking was his demonstration that sometimes the same basal group could produce more than one biological effect. To such groups he gave the name of 'pass keys.' You may ask why should the body trouble to make a more elaborate and no more effective hormone than Professor Dodds can make in his laboratory. I have already given the answer in another connection; it is because the body has to carry out the reactions at a given temperature of 98·4° F. and with severe limitations as to acidity or alkalinity. Many of the laboratory procedures would be incompatible with the life of the cell.

Potency of the Minute Dose

The therapeutic effects of vitamins and hormones illustrate another point—the potency of the minute dose. When someone asked me how I imagined that I could produce any influence on the body by giving five grains of a drug, I replied that the body itself worked with fractions of a milligram. The potency of a hormone is enormous. Abel's extract of the posterior lobe of the pituitary can produce contraction of the uterus when one part is dissolved in 15,000 million parts of water—one grain in 1,000 tons of fluid! This might be claimed as a point for homoeopathy. There is no doubt that Hahnemann had some valuable ideas, even if some of his premises were faulty. The symptom as an expression of something which needed to be assisted rather than repressed; the value of expectant treatment; the efficacy of small doses—all these were progressive conceptions. The whole system of active immunisation by vaccines is based upon aiding the symptomatic expression of the body's attempts to throw off the disease. But, to my mind, the homoeopathic ideal has been spoiled by being crystallised into a creed. That is fatal to progress.

"In the same way the teachings of Galen were crystallised into an almost Athanasian creed for more than 1,000 years—men were actualy killed for disputing his authority. The great Vesalius was sent by the Pope to do penance at Jerusalem for doubting some statements made by Galen, which we now know were quite wrong, and was drowned on his return voyage. We must beware of the dead hand of authority. You have only to refer to some earlier editions of the British Pharmacopoeia to see how many useless drugs were retained in it because of the influence of past authorities. And so I will conclude with a characteristic quotation from my friend and former colleague, Professor Fraser, which I think sums up the present position:—

"'There can be little doubt that we are living in a phase of great advance, on the upstroke of a steep rise in the curve of therapeutic progress, but as we view the history of past progress and allow our imaginations to roam to the centuries ahead we must admit that we are very ignorant and that treatment of disease is in its childhood. If it is in its childhood now, it is our duty to see that it grows up strong and healthy, and, above all, honest.'"

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SHEEP SCAB

The sheep scab position in Great Britain, although showing some improvement, must still be considered as unsatisfactory. Up to the end of October, a correspondent informs us, the total number of confirmed outbreaks during the current year amounted to 141, as compared with 214 in 1939, 130 in 1938, and 175 in 1937, for the corresponding periods. Certainly the situation is relatively better than it was last year, but the persistence of sheep scab on such a scale in this country must cause uneasiness to many thoughtful stock-owners. . . . Perhaps if sheep farmers in certain areas would co-operate fully with the Ministry's veterinary inspectors, there would be less trouble with sheep scab; and increased penalties for failure to report the disease might encourage prompt reporting of cases which would enable more effective steps to be taken to stamp out the disease.—*Scottish Farmer.*

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HEALTH AFTER THE WAR

Medical Commission to Prepare Reforms

A Medical Planning Commission has been set up by the British Medical Association "to study war-time developments and their effects on the country's medical services, both present and future." It will consist of 68 doctors, representing all branches of the profession, under the presidency of Colonel Thomas Fraser, consulting physician to the Aberdeen Royal Infirmary.

In deciding the size and choosing the personnel of the commission the association has had the view that such a body will be in the nature of an assembly, meeting from time to time to debate large questions of principle. The detailed work of the commission will be undertaken in committees and sub-committees, and their resolutions and recommendations will come for discussion before the commission itself.

The association believes that any disadvantage which may be attached to the size of the commission will be more than offset by the advantage of its fully representative character. Much thought has been given to the age distribution of members.

The Chairman of the Council will be Mr. H. S. Souttar, Surgeon to the London Hospital. The English Royal Colleges and the Scottish Royal Corporations are co-operating, and Dr. F. M. B. Allen, Hon. Secretary of the Northern Ireland Branch of the B.M.A., is among the members.

Others include Sir Francis Fremantle, M.P., and Dr. Haden Guest, M.P., of the Parliamentary Medical Committee, and Lord Dawson of Penn, the King's Physician. The Medical Women's Federation is represented. The Ministry of Health and the Department of Health for Scotland have been invited to appoint observers.

Defects of Present Systems

Commenting on the appointment, the *British Medical Journal* says: "The commission has a great opportunity and an equally great responsibility—an opportunity to seize with both hands and a responsibility to call for much searching of heart and mind. It has among its numbers men of all shades of medical experience, and, incidentally, many who are well below the Psalmist's three score years and ten. Those who are to live and to work in the future must have a prominent voice in deciding what that future shall be.

"The commission in its full assembly is to be no more—and no less—than a forum for the discussion of the hard facts collected and classified by the committees and sub-committees formed from its number. The commission is to be the market place in which its members, as sound Athenians, will discuss what is new and reject what is false.

"War has thrown up into sharp relief the deficiencies of our peace-time system of administering relief to the sick and of promoting and maintaining the health of the people.

"The B.M.A. now proposes to prepare for the return of peace so that medicine may be ready to meet its responsibilities in a world in which many values will be changed, fresh conceptions of society will be formed, and in which new stresses and strains will appear in the moral, material and economic fabric of the democracy we hold to be our rightful heritage."

CORRESPONDENCE

Letters to the Editor should reach the Office not later than by the first post on Tuesday morning for insertion in following Saturday's issue.

The views expressed in letters addressed to the Editor represent the personal view of the writer only and must not be taken as expressing the opinion or having received the approval of the N.V.M.A.

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STRAINED TENDONS AND THEIR TREATMENT

To the Editor of the Veterinary Record.

Sir,—Mr. Catmur is the only one who has suggested treatment for my hypothetical case of severe breakdown in a racehorse, and as he condemns his own proposals as unsatisfactory to the owner and to the veterinary surgeon I need not damn them further except to say that the method would undoubtedly result in renewed strain and acute pain when the animal was once more raced over a jumping course if this strain had not occurred during the training period.

It would seem to be generally agreed that bandaging and rest are satisfactory treatments for animals that are to be used for slow work, but the discussion that has been taking place in the columns of the *Veterinary Record* and at the Royal Counties' meeting at Reading has not brought to light any treatment that I or my colleagues could use with confidence, in place of a judicious combination of the methods of firing and blistering, to enable thoroughbreds or hunters with severely strained tendons to return to racing or hunting with satisfaction to the owner, the veterinary surgeon and, presumably, the horse.

The Chantilly veterinary surgeons are, or were, extremely efficient in the use of the firing iron, and their work was characterised by the closeness and neat alignment of the lines or points. Mr. Irving's statement that he has never seen a fired horse in France may be perfectly true, but does not belie the fact that the method was recently popular there for the treatment of strains and for the strengthening of weak joints in thoroughbred horses. On the other hand it is impossible to believe that a man of Mr. Irving's experience could really mean that he has seldom or never seen strain of the flexor tendons in cart horses. Such a remarkable assertion should not be allowed to pass unchecked and I am glad that Mr. Male has pointed out that Mr. Irving's letter is self-contradictory on this subject. His equally categorical statement that he has never found sidebones to cause lameness is difficult to digest and I feel it my duty to add my incredulity to that expressed by Mr. Mayall and Mr. Male. In these days, when the teaching at some of the colleges is known to be weak in large-animal surgery, it is a serious matter that students should be misled by statements such as these appearing in the *Veterinary Record* over the ignature of a veterinary surgeon who is known to have spent a lifetime amongst horses.

It is interesting to note that the French do not consider sidebones as an unsoundness and one reason for the world supremacy of the British breeds of heavy horse may well be that the British breed societies have largely eliminated any tendency to early ossification of the sidebones by breeding from stock that is known to be free of this condition.

Criticism of firing and blistering based on tentative expeditions into the realms of histology have missed the point that the changes caused in the skin by the burning are not important. What really matters is the reaction caused in the tendons themselves, as described in my original article on strained tendons. I do not attach much importance to the scars of line firing acting as a supporting bandage. A violent reaction is required and this is most satisfactorily obtained by firing with fine copper pins right into the substance of the tendons. This allows the blistering ointment, which is applied immediately afterwards, to penetrate through the skin and to inflame the deeper tissues, the object of the treatment being to cure by inflammation. This may sound very drastic, but, as I have said before, the animal is not caused any severe pain, probably because the resultant swelling deadens the nerve endings. A parallel effect is seen in the relief obtained when a blister is applied to a horse showing acute pain in the region of a joint. Relief occurs with the swelling of the part and may be so marked that the animal will bear weight on the affected limb which was previously carried.

I am not as a rule in favour of firing tendons that are not severely strained. In cases that are only showing signs of giving way, or for legs that indicate impending trouble by heat of the part, one of the many preparations of leg paint or blister may be used with satisfactory results and I have treated many horses successfully in this way. I have no doubt that irradiation as used by the late Mr. Cundell, sea water bathing, massage or bandaging combined with rest would be beneficial and would give satisfactory cures in many cases. As for the secret injection used by the French veterinary surgeon, Carnus, I have little doubt that this was a cocaine solution the use of which was fully reported by another French veterinary surgeon of the same name (but, I believe, not related), who claimed 14 per cent. of successful results for the method in selected cases. The Carnus who used this secret remedy over here made ridiculous and exaggerated claims for his treatment and I had the satisfaction of firing several horses which he had selected as most suitable for his injections but which had failed to benefit from them.

To quote from my September article, "Many cases answer to milder treatments, but if these fail, firing and blistering may be superimposed."

Yours faithfully,

A. C. Fraser.

The Veterinary Establishment,
Lambourn, Berks.
January 6th, 1941.

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To the Editor of the Veterinary Record.

Sir,—The correspondence on the subject of firing and strained tendons, in your columns during the past few weeks, will have aroused widespread interest throughout the profession.

May I suggest that a good deal of light would be thrown on the problem by an actual study of the microscopic changes taking place in tendons after "skin firing," and I feel sure that two such experiments, carried out at different institutions, would prove of great value, and could be executed easily. The matter has no doubt been studied naked-eye by many practitioners, for Mr. Male records that he has examined such dead legs, but there must be many students who wonder how deeply, *i.e.*, to what degree of penetration from without inwards, the effects of skin firing can be observed; therefore, rather than draw a simile between the repair of corneal tissue and the probable repair of a "fired tendon" why not do it and see the effects both macro- and microscopically?

Several years ago Dr. A. Piney, of the Cancer Hospital Research Department, carried out some experiments in rabbits in which he found that turpentine injections were followed by the formation of sterile abscesses (free of neutrophiles) composed mainly of lymphocytes. Since it is generally agreed that skin firing does not produce as beneficial effects as point firing, where deeper structures are involved, would there not perhaps be a better response to the local injection of a graduated dose of an irritant such as turpentine?

With reference to the subject of pain following firing it must not be forgotten that the pain associated with the post-firing oedema and inflammation, though less acute than that due to the direct effects of the hot iron on the terminations of the nerve fibres, is nevertheless of importance, and succeeds by some considerable time the effects of local anaesthesia.

Yours faithfully,

W. P. Blount,
Capt., R.A.V.C. (T.A.).

Churt,
Surrey.
December 27th, 1940.